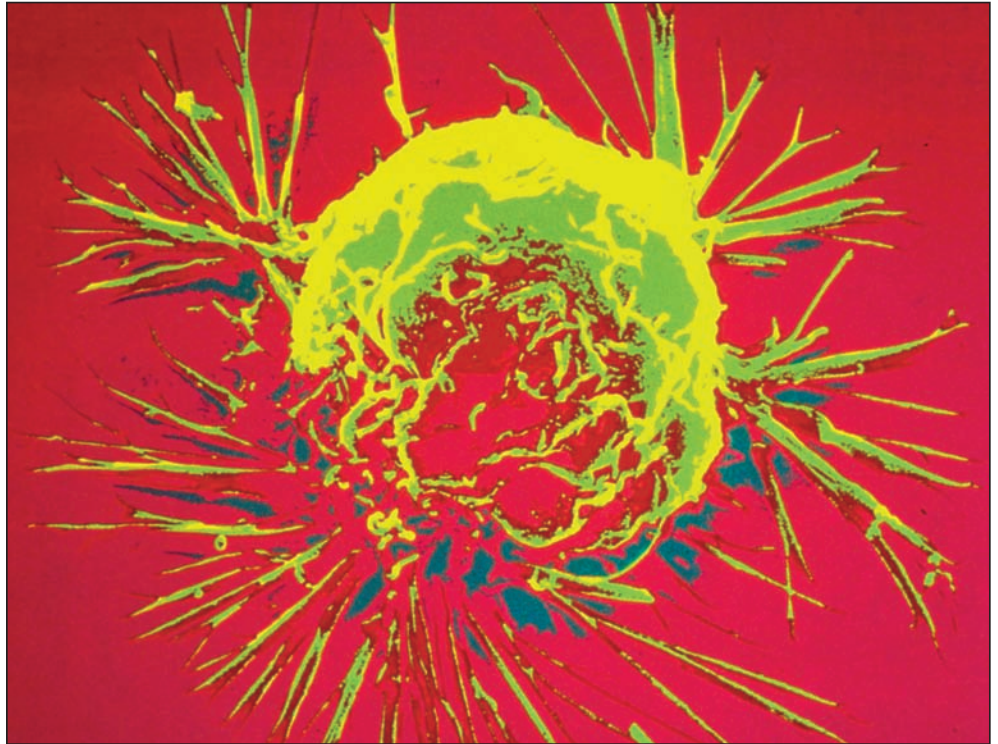


What You Need to Know

- Cancer is a collection of diseases characterized by uncontrolled cell growth.
- This abnormal growth is due to mutations in genes that regulate when and how often a cell divides.
- Most of these mutations are not inherited from parents, but are acquired over our lifetime.
- A number of environmental risks, such as smoking and UV light, can initiate the DNA damage.
- Multiple mutations are required to convert a normal cell to a cancerous tumor.
- Identifying which mutations are present in the cancer offers physicians clues to both outcome and treatment options.
- A number of medications have been developed based on our understanding of the genetic path that is disrupted during the cancer's progression.
- HudsonAlpha and associate companies are engaged in a number of research-, diagnostic- and treatment-based cancer applications.

BIOTECH 101

Cancer



Electron micrograph of a single cell of breast cancer. Image courtesy of the National Cancer Institute

If you want to know more:

American Cancer Society
www.cancer.org

CancerQuest
www.cancerquest.org

Conversant Healthcare, Inc.
www.conversanthcs.com

Applied Genomics, Inc.
www.applied-genomics.com

Expression Genetics, Inc.
www.egencorp.com

New Century Pharmaceuticals
www.newcenturypharm.com

Of all the disorders, diseases and illnesses, few today are as universally feared as cancer. More than 1,500 Americans die from cancer each day. In the United States, the lifetime risk of developing cancer is nearly 1 in 2 for men and slightly more than 1 in 3 for women. The American Cancer Society estimates in Alabama alone, 22,340 individuals will develop some form of cancer this year.

What is Cancer?

Cancer is a collection of diseases characterized by an uncontrolled growth of cells and their spread to surrounding tissues. Although each cancer type is somewhat unique, there are several common features among cancers. Nearly all types are genetic in nature – that is, cancer is caused by changes in the genes that control cell growth and division. Some changes occur in genes that are normally

involved in stimulating cells to divide. The mutated form of these genes, called oncogenes, lead to over-stimulation and increased cell division. Think about a gas pedal on a car being stuck in the “on” position. Another group of genes known as tumor suppressors produce proteins that normally block cell division. Continuing the car analogy, mutations in tumor suppressors remove these blocks, similar to cutting the brake lines.

While all cancers involve mutations in both oncogenes and tumor suppressors, only about 5 percent have a strong hereditary component. In these rare cases, the cancer is primarily caused by mutations inherited from a parent. Most cancers do not result from inherited mutations, but are due to an accumulation of DNA damage acquired during our lifetime. These cancers begin with a single “starting” cell that becomes

genetically damaged. The transformation from that initial cell into a tumor is a stepwise progression. As shown in figure one, when the cell undergoes multiple rounds of growth and division, the resulting 'daughter' cells often acquire additional mutations in other oncogenes or tumor suppressors. These cells become progressively more abnormal, ultimately invading surrounding tissues and/or spreading to other parts of the body (metastasis). The number of genetic mutations that are required to convert a genetically normal cell into a metastatic tumor varies with cancer type. These genetic changes may involve single "letter" substitutions, large deletions or duplications or chromosomal rearrangements impacting vast sections of the genome.

Initiating Factors

Although some fraction of genetic mutation may occur by random chance, many cancer-causing mutations begin with an initiator. The initiator is often a chemical compound that reacts with the DNA. Alcohol, asbestos and benzo(a) pyrene, a chemical found in cigarette smoke, are all known initiators. UV radiation is another initiator and a cause of skin cancer. Certain viruses and bacteria have also been associated with tumor initiation. For example, the human

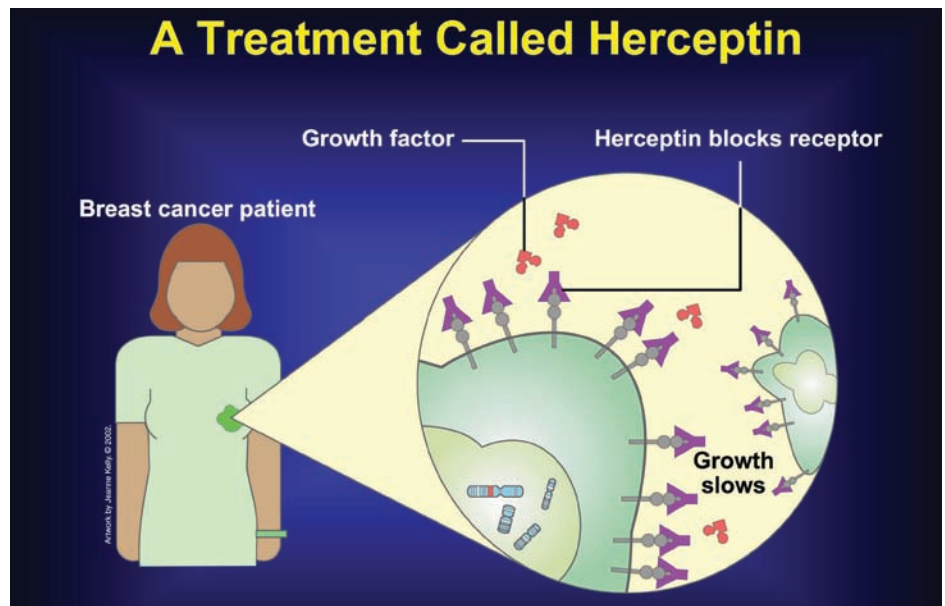


Figure 2 – Herceptin binds breast cancer HER2 receptors and blocks growth. Illustration courtesy of the National Cancer Institute

papillomavirus (HPV) is the greatest risk factor associated with cervical cancer. Prolonged exposure to these initiators greatly increases the likelihood a cancer will form.

Several of these risk factors can be controlled. Scientists estimate that as many as 50 to 75 percent of cancer deaths in the U.S. are caused by human behaviors such as smoking, physical inactivity, poor dietary choices and sun exposure.

Cancer Diagnosis and Treatment: Then and Now

Historically, the diagnosis of cancers

has been based on visual evaluation and staging as determined by cell appearance and spread to nearby or distant tissues. Treatment decisions and options are often based upon this information. In many cases, however, individuals with similar-appearing tumors will show markedly different responses to treatment. This suggests that differences at the molecular level may be responsible for varying outcomes. Increasingly, oncologists are adding molecular analysis of a patient's cancer as part of a standard diagnostic workup. Such tests may include:

Gene expression profiling measures the activity (or expression) of thousands of genes simultaneously within a cancer. Experiments of this kind are often able to sort patients into groups based on which genes are active and their level of activity. Often, the groups will show differences in response to a certain treatment or overall survival. If validated, these differences can be used to predict outcomes for new patients, helping physicians identify the most optimal treatment or course of action.

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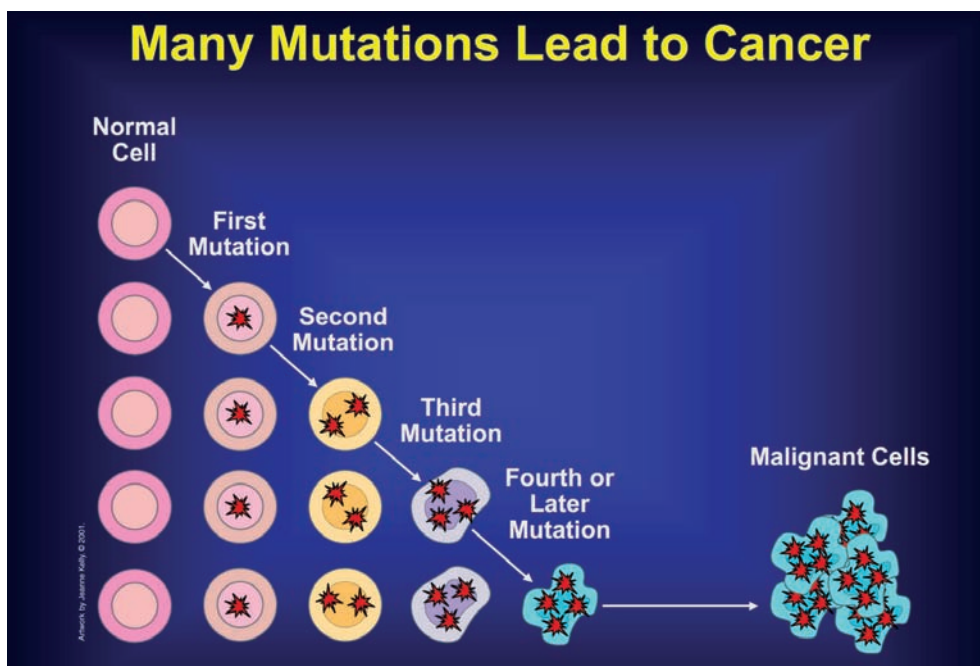


Figure 1 – Progression to cancer involves many genetic mutations over time. Illustration courtesy of the National Cancer Institute

BIOTECH 101 CONTINUED :

Immunohistochemical testing is another method to measure gene activity, but at a much narrower level, usually on the order of 10 genes or fewer at one time. This method detects the presence of specific proteins within the cancer. For example, the receptors for estrogen, progesterone and HER2 growth factors are often identified immunohistochemically in breast cancer biopsies. Detecting whether each receptor is present and at what level becomes useful in determining which therapy will be most effective.

Understanding the molecular makeup of a cancer may lead to a specific drug being used in treatment. The field of pharmacogenomics deals with how a patient's specific genetic variation (or in this case, the cancer's specific variation) affects the response to certain drugs. For example, if the HER2 receptor described above is present at high levels on a breast cancer tumor, the anti-cancer drug Herceptin® is added to the patient's treatment plan. Herceptin® binds the HER2 receptor and increases the efficacy of chemotherapy (figure 2). In a similar manner, Gleevec® and Erbitux® may be prescribed for specific forms of chronic myeloid leukemia and colorectal cancer, respectively. Therapy based on molecular targets is slowly but surely gaining in acceptance as additional genetic cancer pathways are identified.

– Dr. Neil Lamb

director of educational outreach
HudsonAlpha Institute for
Biotechnology